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FILE 'HOME' ENTERED AT 09:37:23 ON 28 DEC 2000

=> file medline biosis embase caplus

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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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FILE 'BIOSIS' ENTERED AT 09:37:37 ON 28 DEC 2000
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=> s neural (s) stem (s) cell (p) treatment

   3 FILES SEARCHED...
L1          208 NEURAL (S) STEM (S) CELL (P) TREATMENT

=> s neural (s) stem (s) cell (p) treatment (p) difficult

   3 FILES SEARCHED...
L2            2 NEURAL (S) STEM (S) CELL (P) TREATMENT (P) DIFFICULT

=> d l2 total ibib kwic


L2   ANSWER 1 OF 2  MEDLINE
ACCESSION NUMBER:   1999444590      MEDLINE
DOCUMENT NUMBER:    99444590
TITLE:              Prospects for the clinical application of neural
                    transplantation with the use of conditionally immortalized
                    neuroepithelial stem cells.
AUTHOR:             Gray J A; Hodges H; Sinden J
CORPORATE SOURCE:   Department of Psychology, Institute of Psychiatry, London,
                    UK.
SOURCE:             PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON.
                    SERIES B: BIOLOGICAL SCIENCES, (1999 Aug 29) 354 (1388)
                    1407-21.  Ref: 87
                    Journal code: P5Z. ISSN: 0962-8436.
PUB. COUNTRY:       ENGLAND: United Kingdom
                    Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200001
ENTRY WEEK:         20000104
AB   Although neural transplantation has made a relatively successful
     transition from the animal laboratory to human neurosurgery for the
     treatment of Parkinson's disease, the use of human embryonic brain
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tissue as the source of transplants raises **difficult** ethical and practical problems. These are likely to impede the widespread use of this otherwise promising therapy across the range. . . needed, so obviating the requirement for fresh embryonic tissue at each occasion of surgery. Particularly promising are conditionally immortalized neuroepithelial **stem cell** lines in which the immortalizing gene is downregulated upon transplantation into a host brain. We describe experiments from our laboratory with the use of **cells** of this kind, the multipotent MHP clonal **cell** lines, derived from the developing hippocampus of a transgenic mouse harbouring a temperature-sensitive oncogene. Implanted into the hippocampus of rats and marmosets with damage to the CA1 **cell** field, the MHP36 line gave rise to healthy surviving grafts and to essentially complete recovery of cognitive function. Postmortem study of the implanted rat brains indicated that MHP36 **cells** migrate to the region of damage, adopt both neuronal (pyramidal) and glial phenotypes in vivo, and reconstitute the normal laminated appearance of the CA1 **cell** field. We have previously shown that, when primary differentiated foetal tissue is used as the source of grafts in rats with CA1 damage, there is a stringent requirement for replacement with homotypic CA1 **cells**. We interpret our results as showing that the MHP36 **cell** line responds to putative signals associated with damage to the hippocampus and takes up a phenotype appropriate for the repair. . . of this damage; they therefore open the way to the development of a novel strategy with widespread applicability to the **treatment** of the diseased or damaged human brain.

L2 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:491215 BIOSIS
DOCUMENT NUMBER: PREV199900491215
TITLE: Prospects for the clinical application of neural transplantation with the use of conditionally immortalized neuroepithelial stem cells.
AUTHOR(S): Gray, Jeffrey A. (1); Hodges, Helen; Sinden, John
CORPORATE SOURCE: (1) Department of Psychology, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London, SE5 8AF UK
SOURCE: Philosophical Transactions of the Royal Society of London B Biological Sciences, (Aug., 1999) Vol. 354, No. 1388, pp. 1407-1421.
ISSN: 0962-8436.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although **neural** transplantation has made a relatively successful transition from the animal laboratory to human neurosurgery for the **treatment** of Parkinson's disease, the use of human embryonic brain tissue as the source of transplants raises **difficult** ethical and practical problems. These are likely to impede the widespread use of this otherwise promising therapy across the range. . . needed, so obviating the requirement for fresh embryonic tissue at each occasion of surgery. Particularly promising are conditionally immortalized neuroepithelial **stem cell** lines in which the immortalizing gene is downregulated upon transplantation into a host brain. We describe experiments from our laboratory with the use of **cells** of this kind, the multipotent MHP clonal **cell** lines, derived from the developing hippocampus of a transgenic mouse harbouring a temperature-sensitive oncogene. Implanted into the hippocampus of rats and marmosets with damage to the CA1 **cell** field, the MHP36 line gave rise to healthy surviving grafts and to essentially complete recovery of cognitive function. Postmortem study of the implanted rat brains indicated

that MHP36 **cells** migrate to the region of damage, adopt both neuronal (pyramidal) and glial phenotypes in vivo, and reconstitute the normal laminated appearance of the CA1 **cell** field. We have previously shown that, when primary differentiated foetal tissue is used as the source of grafts in rats with CA1 damage, there is a stringent requirement for replacement with homotypic CA1 **cells**. We interpret our results as showing that the MHP36 **cell** line responds to putative signals associated with damage to the hippocampus and takes up a phenotype appropriate for the repair of this damage; they therefore open theway to the development of a novel strategy with widespread applicability to the **treatment** of the diseased or damaged human brain.

```
=> s neural (s) stem (s) cell (p) treatment (p) pharmaceut?

   2 FILES SEARCHED...
   3 FILES SEARCHED...
L3            2 NEURAL (S) STEM (S) CELL (P) TREATMENT (P) PHARMACEUT?

=> dup rem l3

PROCESSING COMPLETED FOR L3
L4             2 DUP REM L3 (0 DUPLICATES REMOVED)

=> d l4 total ibib kwic


L4   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         2000:368139  CAPLUS
DOCUMENT NUMBER:          132:343355
TITLE:                    Growth hormone-modulating agents and method for
                          treatment of conditions affecting neural stem cells
or
                          progenitor cells
INVENTOR(S):              Eriksson, Peter
PATENT ASSIGNEE(S):       A+ Science Invest AB, Swed.
SOURCE:                   PCT Int. Appl., 22 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2000030675      A2   20000602       WO 1999-SE2197    19991125
     WO 2000030675      A3   20000817
         W:  AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                       SE 1998-4064     19981125
AB   The invention discloses the use of a substance that, on administration,
     will lead to increased concns. of growth hormone, e.g. growth hormone, a
     functionally equiv. analog thereof, or a substance that will increase the
     release of endogenous growth hormone, for the prodn. of a medicinal
     product for treatment of abnormal conditions affecting
     neural stem cells, progenitor cells
     and/or cells derived from neural stem
```

cells or progenitor **cells**, esp. conditions affecting the oligodendroglia, astroglia, and/or neuronal **cells**. In vitro and in vivo methods are disclosed for inducing lineage detn., propagating and/or inducing or maintaining the genesis of neurons, oligodendrocytes, astroglial cells from progenitor cells, stem cells and/or cells derived from said cells by administering to the cells a substance that increases the concn. of growth hormone. Also disclosed is a method of reducing the genesis of oligodendrocytes, neurons, or astroglial cells from progenitor cells or stem cells, wherein a **pharmaceutically** effective amt. of a substance that will lead to a decreased concn. of growth hormone or a functionally equiv. analog thereof is administered to the patient.

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:595378 CAPLUS
DOCUMENT NUMBER: 131:210090
TITLE: Protein and cDNA sequences for a human fibroblast growth factor (FGF 98), and uses thereof in the diagnosis and treatment of degenerative diseases
INVENTOR(S): Cen, Hui; Garcia, Pablo D.; Grieshammer, Uta; Kassam, Altaf; Lee, Pauline P.; Pot, David; Gospodarowicz, Denis; Martin, Kathleen
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9946381	A2	19990916	WO 1999-US5235	19990309
WO 9946381	A3	19991104		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9930760	A1	19990927	AU 1999-30760	19990309
PRIORITY APPLN. INFO.:			US 1998-77411	19980309
			US 1998-83553	19980429
			US 1999-264851	19990308
			WO 1999-US5235	19990309

AB This invention provides protein and cDNA sequences for a newly identified human protein, designated FGF 98, which is a member of the fibroblast growth factor (FGF) family. In a preferred embodiment, primary central (CNS) and peripheral nervous system (PNS) cells, when treated with FGF 98 of the invention, proliferate, have at least a limited self regeneration capacity, and can undergo lineage restriction in response to the local environment. Although FGF 98 has been described on the basis of its ability to promote the survival of neuronal cell types, this factor will act on other neuronal cell types as well. The invention provides methods of using FGF 98 for the isolation, regeneration, proliferation, and differentiation of mammalian multipotent **neural stem cells**, progenitor **cells**, and progeny. In a further embodiment, cells produced by **treatment** with FGF 98 are used to screen drugs which may affect development, differentiation, survival, and/or function of CNS and PNS derived neurons and glia. The invention also includes therapeutic or **pharmaceutical** compns. comprising FGF 98 in a effect amt. for treating patients with degenerative diseases. In one embodiment, FGF 98 may be therapeutically administered by implanting into patients vectors or cells capable of producing a

biol.-active form of FGF 98 or a precursor of FGF 98.

=> s neural (s) stem (s) cell (p) treatment (p) implant?

2 FILES SEARCHED...
L5 12 NEURAL (S) STEM (S) CELL (P) TREATMENT (P) IMPLANT?

=> dup rem l5

PROCESSING COMPLETED FOR L5
L6 6 DUP REM L5 (6 DUPLICATES REMOVED)

=> d l6 total ibib kwic

L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:241442 CAPLUS
DOCUMENT NUMBER: 132:247142
TITLE: Engraftable neural progenitor and stem cells for brain tumor therapy
INVENTOR(S): Snyder, Evan Y.; Lynch, William P.; Breakefield, Xandra O.; Aboody, Karen
PATENT ASSIGNEE(S): The Children's Hospital Medical Center Corp., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020560	A1	20000413	WO 1999-US21311	19990917
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1036162	A1	20000920	EP 1999-946954	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-168350 19981007
WO 1999-US21311 19990917

REFERENCE COUNT: 6
REFERENCE(S):
(1) Barba; J Neurosurg 1993, V79, P729 CAPLUS
(2) Flax; Nature Biotechnology 1998, V16, P1033 CAPLUS
(4) Svendsen, C; Review Article:Neural stem cells for brain repair Alzheimer's Research 1997, V3, P131 CAPLUS
(5) Takamiya; J Neurosurg 1993, V79, P104 MEDLINE
(6) Weiss; US 5750376 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB One of the impediments to the **treatment** of some human brain tumors (e.g., gliomas) has been the degree to which they expand, migrate widely, and infiltrate normal tissue. We demonstrate that a clone of multipotent **neural** progenitor **stem cells**, when **implanted** into an exptl. glioma, will migrate along with and distribute themselves throughout the tumor in juxtaposition to widely expanding and aggressively advancing tumor **cells**, while continuing to express a foreign reporter gene. Furthermore, drawn somewhat by the degenerative environment created just beyond the infiltrating tumor edge, the neural progenitor cells migrate slightly beyond and surround the invading tumor border. When **implanted** at a distant site from the tumor bed (e.g., into normal tissue, into the contralateral hemisphere, into the lateral ventricles) the donor

neural progenitor/**stem cells** will migrate through normal tissue and specifically target the tumor **cells**. These results suggest the adjunctive use of **neural** progenitor/**stem cells** as a novel, effective delivery vehicle for helping to target therapeutic genes and vectors to invasive brain tumors that have been refractory to **treatment**.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:878431 CAPLUS
TITLE: Transplanted fetal striatum in Huntington's disease: Phenotypic development and lack of pathology
AUTHOR(S): Freeman, Thomas B.; Cicchetti, Francesca; Hauser, Robert A.; Deacon, Terrence W.; Li, Xiao-Jiang; Hersch, Steven M.; Nauert, G. Michael; Sanberg, Paul R.; Kordower, Jeffrey H.; Saporta, Samuel; Isacson, Ole
CORPORATE SOURCE: Department of Neurosurgery, Department of Pharmacology and Experimental Therapeutics, and The Neuroscience Program, University of South Florida, Tampa, FL, 33606, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (2000), 97(25), 13877-13882
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Neural** and **stem cell** transplantation is emerging as a potential **treatment** for neurodegenerative diseases. Transplantation of specific committed neuroblasts (fetal neurons) to the adult brain provides such scientific exploration of these new potential therapies. Huntington's disease (HD) is a fatal, incurable autosomal dominant (CAG repeat expansion of huntingtin protein) neurodegenerative disorder with primary neuronal pathol. within the caudate-putamen (striatum). In a clin. trial of human fetal striatal tissue transplantation, one patient died 18 mo after transplantation from cardiovascular disease, and postmortem histol. anal. demonstrated surviving transplanted cells with typical morphol. of the developing striatum. Selective markers of both striatal projection and interneurons such as dopamine and c-AMP-related phosphoprotein, calretinin, acetylcholinesterase, choline acetyltransferase, tyrosine hydroxylase, calbindin, enkephalin, and substance P showed pos. transplant regions clearly innervated by host tyrosine hydroxylase fibers. There was no histol. evidence of immune rejection including microglia and macrophages. Notably, neuronal protein aggregates of mutated huntingtin, which is typical HD neuropathol., were not found within the transplanted fetal tissue. Thus, although there is a genetically predetd. process causing neuronal death within the HD striatum, **implanted** fetal neural cells lacking the mutant HD gene may be able to replace damaged host neurons and reconstitute damaged neuronal connections. This study demonstrates that grafts derived from human fetal striatal tissue can survive, develop, and are unaffected by the disease process, at least for 18 mo, after transplantation into a patient with HD.

L6 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 2001:7647 BIOSIS
DOCUMENT NUMBER: PREV200100007647
TITLE: Neural stem cells display extensive tropism for pathology in adult brain: Evidence from intracranial gliomas.
AUTHOR(S): Aboody, Karen S.; Brown, Alice; Rainov, Nikolai G.; Bower, Kate A.; Liu, Shaoxiong; Yang, Wendy; Small, Juan E.; Herrlinger, Ulrich; Ourednik, Vaclav; Black, Peter McL.; Breakefield, Xandra O.; Snyder, Evan Y. (1)
CORPORATE SOURCE: (1) Departments of Neurology, Pediatrics, and Neurosurgery, Children's Hospital, Harvard Medical School, Boston, MA,

02115: Snyder@A1.TCH.Harvard.edu USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (November 7, 2000) Vol. 97, No. 23, pp. 12846-12851. print.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB One of the impediments to the **treatment** of brain tumors (e.g., gliomas) has been the degree to which they expand, infiltrate surrounding tissue, and migrate widely into normal brain, usually rendering them "elusive" to effective resection, irradiation, chemotherapy, or gene therapy. We demonstrate that **neural stem cells** (NSCs), when **implanted** into experimental intracranial gliomas in vivo in adult rodents, distribute themselves quickly and extensively throughout the tumor bed and migrate uniquely in juxtaposition to widely expanding and aggressively advancing tumor **cells**, while continuing to stably express a foreign gene. The NSCs "surround" the invading tumor border while "chasing down" infiltrating tumor **cells**. When **implanted** intracranially at distant sites from the tumor (e.g., into normal tissue, into the contralateral hemisphere, or into the cerebral ventricles), the donor **cells** migrate through normal tissue targeting the tumor **cells** (including human glioblastomas). When **implanted** outside the CNS intravascularly, NSCs will target an intracranial tumor. NSCs can deliver a therapeutically relevant molecule-cytosine deaminase-such that quantifiable. . .

L6 ANSWER 4 OF 6 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000207091 MEDLINE
DOCUMENT NUMBER: 20207091
TITLE: Gene therapy of experimental brain tumors using neural progenitor cells [see comments].
COMMENT: Comment in: Nat Med 2000 Apr;6(4):369-70
AUTHOR: Benedetti S; Pirola B; Pollo B; Magrassi L; Bruzzone M G; Rigamonti D; Galli R; Selleri S; Di Meco F; De Fraja C; Vescovi A; Cattaneo E; Finocchiaro G
CORPORATE SOURCE: Istituto Nazionale Neurologico Besta, via Celoria 11, 20133
Milano, Italy.
SOURCE: NATURE MEDICINE, (2000 Apr) 6 (4) 447-50.
Journal code: CG5. ISSN: 1078-8956.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY WEEK: 20000803
AB . . . Gene therapy of glioblastomas is limited by the short survival of viral vectors and by their difficulty in reaching glioblastoma **cells** infiltrating the brain parenchyma. **Neural stem**/progenitor **cells** can be engineered to produce therapeutic molecules and have the potential to overcome these limitations because they may travel along the white matter, like neoplastic **cells**, and engraft stably into the brain. Retrovirus-mediated transfer of the gene for interleukin-4 is an effective **treatment** for rat brain glioblastomas. Here, we transferred the gene for interleukin-4 into C57BL6J mouse primary **neural** progenitor **cells** and injected those **cells** into established syngeneic brain glioblastomas. This led to the survival of most tumor-bearing mice. We obtained similar results by **implanting** immortalized **neural** progenitor **cells** derived from Sprague-Dawley rats into C6 glioblastomas. We also documented by magnetic resonance imaging the progressive disappearance of large tumors, and

detected 5-bromodeoxyuridine-labeled progenitor **cells** several weeks after the injection. These findings support a new approach for gene therapy of brain tumors, based on the grafting of **neural stem cells** producing therapeutic molecules.

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:595378 CAPLUS
DOCUMENT NUMBER: 131:210090
TITLE: Protein and cDNA sequences for a human fibroblast growth factor (FGF 98), and uses thereof in the diagnosis and treatment of degenerative diseases
INVENTOR(S): Cen, Hui; Garcia, Pablo D.; Grieshammer, Uta; Kassam, Altaf; Lee, Pauline P.; Pot, David; Gospodarowicz, Denis; Martin, Kathleen
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9946381	A2	19990916	WO 1999-US5235	19990309
WO 9946381	A3	19991104		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9930760	A1	19990927	AU 1999-30760	19990309
PRIORITY APPLN. INFO.:			US 1998-77411	19980309
			US 1998-83553	19980429
			US 1999-264851	19990308
			WO 1999-US5235	19990309

AB This invention provides protein and cDNA sequences for a newly identified human protein, designated FGF 98, which is a member of the fibroblast growth factor (FGF) family. In a preferred embodiment, primary central (CNS) and peripheral nervous system (PNS) cells, when treated with FGF 98 of the invention, proliferate, have at least a limited self regeneration capacity, and can undergo lineage restriction in response to the local environment. Although FGF 98 has been described on the basis of its ability to promote the survival of neuronal cell types, this factor will act on other neuronal cell types as well. The invention provides methods of using FGF 98 for the isolation, regeneration, proliferation, and differentiation of mammalian multipotent **neural stem cells**, progenitor **cells**, and progeny. In a further embodiment, cells produced by **treatment** with FGF 98 are used to screen drugs which may affect development, differentiation, survival, and/or function of CNS and PNS derived neurons and glia. The invention also includes therapeutic or pharmaceutical compns. comprising FGF 98 in a effect amt. for treating patients with degenerative diseases. In one embodiment, FGF 98 may be therapeutically administered by **implanting** into patients vectors or cells capable of producing a biol.-active form of FGF 98 or a precursor of FGF 98.

L6 ANSWER 6 OF 6 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999444590 MEDLINE
DOCUMENT NUMBER: 99444590
TITLE: Prospects for the clinical application of neural transplantation with the use of conditionally immortalized

neuroepithelial stem cells.

AUTHOR: Gray J A; Hodges H; Sinden J

CORPORATE SOURCE: Department of Psychology, Institute of Psychiatry, London, UK.

SOURCE: PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON. SERIES B: BIOLOGICAL SCIENCES, (1999 Aug 29) 354 (1388) 1407-21. Ref: 87
Journal code: P5Z. ISSN: 0962-8436.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200001

ENTRY WEEK: 20000104

AB Although **neural** transplantation has made a relatively successful transition from the animal laboratory to human neurosurgery for the **treatment** of Parkinson's disease, the use of human embryonic brain tissue as the source of transplants raises difficult ethical and practical. . . needed, so obviating the requirement for fresh embryonic tissue at each occasion of surgery. Particularly promising are conditionally immortalized neuroepithelial **stem cell** lines in which the immortalizing gene is downregulated upon transplantation into a host brain. We describe experiments from our laboratory with the use of **cells** of this kind, the multipotent MHP clonal **cell** lines, derived from the developing hippocampus of a transgenic mouse harbouring a temperature-sensitive oncogene. **Implanted** into the hippocampus of rats and marmosets with damage to the CA1 **cell** field, the MHP36 line gave rise to healthy surviving grafts and to essentially complete recovery of cognitive function. Postmortem study of the **implanted** rat brains indicated that MHP36 **cells** migrate to the region of damage, adopt both neuronal (pyramidal) and glial phenotypes in vivo, and reconstitute the normal laminated appearance of the CA1 **cell** field. We have previously shown that, when primary differentiated foetal tissue is used as the source of grafts in rats with CA1 damage, there is a stringent requirement for replacement with homotypic CA1 **cells**. We interpret our results as showing that the MHP36 **cell** line responds to putative signals associated with damage to the hippocampus and takes up a phenotype appropriate for the repair. . . of this damage; they therefore open the way to the development of a novel strategy with widespread applicability to the **treatment** of the diseased or damaged human brain.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	58.74	58.95
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.78	-2.78

STN INTERNATIONAL LOGOFF AT 09:51:25 ON 28 DEC 2000